

REMARKS

I. Introduction

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

II. Summary of the Claims and Amendments Thereto

Claims 1 – 9 are requested to be cancelled. In their place, claims 10 – 20 are presented anew, taking into consideration the issues raised by the PTO as discussed below. The following chart shows how the new claims derive support from and correlate to cancelled claims:

New Claim(s)	Old Claim(s)
10, 11	1
12	5
13	6
14	4
15, 16	7
17, 18	8, 9
19, 20	1

Applicants believe that the new claims do not introduce new matter and therefore respectfully request the PTO to enter the claims.

III. The Office Action

A. Rejection of Claims Under 35 U.S.C. § 112, Second Paragraph

1. “Use”

Claims 1 – 9 stand rejected as being allegedly indefinite for reciting a “use without any active, positive steps . . .” Office Action at page 2. Applicants respectfully traverse this rejection to the extent that it may apply to the claims presented anew.

Claims 10 – 20 are plainly directed to methods of use that recite administration steps. Accordingly, Applicants submit that this ground for rejection is moot and respectfully request the PTO to withdraw the rejection.

2. “E.g.”

Claims 5 and 9 are rejected as being allegedly indefinite for their recitations of “e.g.”, which in the PTO’s opinion gives rise to impermissible broad and narrow ranges being recited within the same claim. Office Action at pages 2-3. Applicants respectfully traverse this rejection.

New claims 10 – 20 do not recite “e.g.” or any other simultaneous broad and narrow limitations. Consequently, Applicants submit that this rejection is also moot and respectfully request the PTO to reconsider and withdraw the rejection.

3. “Pure” and “Enriched” Forms

Claim 3 stands rejected as being allegedly indefinite for reciting R enantiomers being used in “pure” or in “enriched” forms. In the PTO’s opinion, these designations are qualitative and, without more definition, cannot be understood. Applicants respectfully traverse this rejection to the extent that it may apply to newly presented claims 10 – 20.

The new claims do not recite the allegedly indefinite terminology. Accordingly, this ground for rejection is moot and Applicants courteously request the PTO to reconsider and withdraw this rejection.

4. “Normally” or “Controlled” Liberating Form

In the PTO’s opinion, claim 4 is indefinite for reciting the phrase “normally liberating or controlled liberating form” and requested Applicants to clarify the same.

Applicants courteously submit that claim 14, which corresponds to cancelled claim 4, is drafted using more conventional terminology in reciting a “normal or controlled release form.” In this regard, Applicants submit that the definition of and distinction between normal and controlled release dosage forms are well-understood in the art. Consequently, a person of

ordinary skill would harbor no uncertainty as to the meaning of “normal” and “controlled release.” Accordingly, Applicants respectfully request the PTO to reconsider and withdraw this rejection.

B. Rejection of Claims Under 35 U.S.C. § 101

Claims 1 – 9 stand rejected as reciting allegedly non-statutory subject matter. Office Action at page 4. The PTO elaborates that the rejected claims are not proper process claims. Applicants respectfully traverse the rejection to the extent that it may apply to new claims 10 – 18.

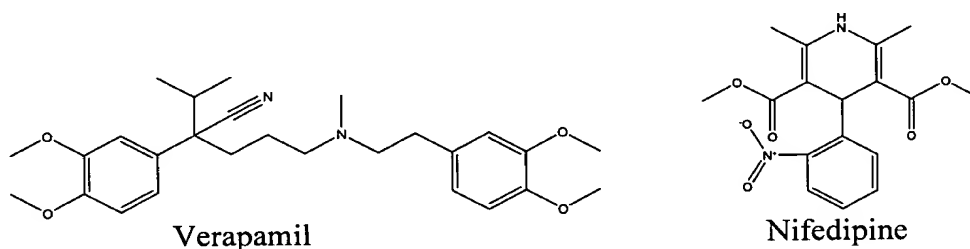
Claims 10 – 20 are drawn properly to methods that fall within the ambit of section 101. Accordingly, Applicants courteously submit that this rejection is moot and request the PTO to reconsider and withdraw the rejection.

C. Rejection of Claims under 35 U.S.C. § 103(a)

Claims 1 – 9 stand rejected as being allegedly obvious over Jouvin-Marche *et al.* (“Jouvin-Marche”). In the PTO’s opinion, Jouvin-Marche discloses Ca^{2+} antagonists such as nifedipine as being useful in inhibiting the secretion of beta-glucuronidase in human neutrophils. Jouvin-Marche further discloses verapamil as a Ca^{2+} antagonist, but does not specifically teach that verapamil or its R-enantiomer actually inhibits beta-glucuronidase. However, the PTO alleges that a person of ordinary skill would have expected that secretion of beta-glucuronidase is “closely related” to the presence of extracellular Ca^{2+} . The PTO also alleges that the person of ordinary skill in the art also would have recognized that inhibition of Ca^{2+} uptake results in the “inhibition of beta-glucuronidase.” Consequently, the PTO concludes that the person of ordinary skill in the art would have used verapamil to inhibit human tissue beta-glucuronidase with the expectation that verapamil, a Ca^{2+} antagonist, would have “similar activities” as the disclosed nifedipine Ca^{2+} antagonist. Additionally, the PTO suggests that the use of a single enantiomer, such as the R enantiomer, of a compound is an obvious use where the racemic mixture of the compound is used. Applicants respectfully traverse this rejection to the extent that it might apply to new claims 10 – 18.

Jouvin-Marche does not teach or suggest the claimed method of treating a subject suffering from a condition that is characterized by high human tissue glucuronidase activity. There is absolutely no suggestion whatsoever in Jouvin-Marche that administration of the recited compounds would give rise to an effective therapy that addresses the presence of glucuronidase in human tissue. The PTO correctly notes that Jouvin-Marche discloses that nifedipine inhibits the *secretion* of glucuronidase. By contrast, the claimed invention provides a method of using verapamil, among others, to treat conditions that arise from the *presence* of glucuronidase in tissues. Jouvin-Marche does not teach or suggest that nifedipine specifically, or even Ca^{2+} inhibitors generally, can be used to inhibit glucuronidase that is *already present and circulated* in tissue.

Even if Jouvin-Marche did teach or suggest that nifedipine or Ca^{2+} inhibitors generally inhibit glucuronidase, a premise that Applicants do not endorse, the person of ordinary skill in the art would have absolutely no expectation that verapamil would inhibit glucuronidase because nifedipine and verapamil are chemically very distinct. The PTO's position appears to rely upon a shared property -- Ca^{2+} inhibition -- between nifedipine and verapamil that purportedly suggests to the artisan the presence of another common property -- glucuronidase inhibition. This cannot be the case. As shown below, nifedipine and verapamil have completely different chemical structures:



A person of ordinary skill would immediately comprehend that any common pharmacological property between the two is coincidental. Furthermore, in the absence of any guiding principle to the contrary, the person would never expect these compounds to necessarily share another but different pharmacological property, here, inhibition of glucuronidase.

Because Jouvin-Marche does not teach or suggest the claimed methods or the underlying glucuronidase inhibitory activity of the compounds recited in the claims, Applicants respectfully submit that the person of ordinary skill would not consider Applicants' invention to be obvious in light of Jouvin-Marche. Accordingly, Applicants respectfully request the PTO to reconsider and withdraw this rejection.

IV. Conclusion

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if he feels that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

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By Steven M. Reid

FOLEY & LARDNER
Washington Harbour
3000 K Street, N.W., Suite 500
Washington, D.C. 20007-5143
Telephone: (202) 295-4767
Facsimile: (202) 672-5399

Steven M. Reid, Ph.D.
Representative for Applicant
Registration No. 54,393

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.